

EXHIBIT D



**ZYPREXA** is indicated for the treatment of –

**Schizophrenia**  
Symptoms include:

delusions  
hallucinations

**Acute bipolar mania**  
Symptoms include:

sleeplessness  
irritability  
aggression

**ZYPREXA**  
Olanzapine

*Lilly*



Predictable symptom control of both psychosis and elevated mood helps you **restore calm.**

Dependable maintenance of treatment response in schizophrenia helps you **bring comfort.**

Flexible dosing helps you **customize care.**

ZYPREXA is indicated for the treatment of schizophrenia and acute bipolar mania.

Caution should be used in dosing to the elderly, especially if there are other factors that might additively influence drug metabolism and/or pharmacodynamic sensitivity.

Restoring  
dignity to residents' lives



Restore calm

Bring comfort

Customize care

**ZYPREXA**  
Olanzapine

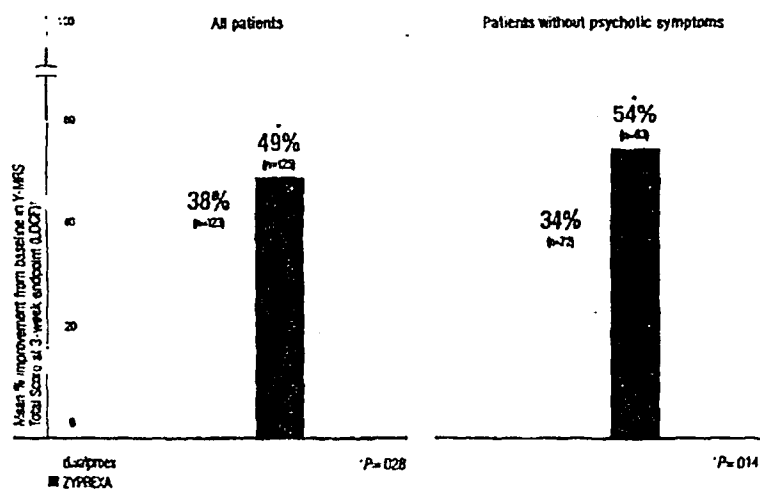
# Bring comfort to residents' lives

## Significantly more patients achieved higher levels of improvement in psychosis compared to risperidone<sup>1</sup>

In a schizophrenia study, a significantly greater percentage of patients treated with ZYPREXA achieved an improvement of  $\geq 40\%$  in PANSS Total Score as compared with risperidone-treated patients. The percentage of patients achieving a 20% improvement in PANSS Total Score was comparable between treatment groups.<sup>1</sup>

<sup>1</sup> Tera PK, et al. *J Clin Psychopharmacol* 1997;17:407-418.  
<sup>†</sup> PANSS is Positive and Negative Syndrome Scale, consisting of 30 items.  
 See page 6 for more information.

## Efficacy in treating symptoms of elevated mood<sup>1,2</sup>



### Symptoms include:

IRRITABILITY

DISRUPTIVE/

AGGRESSIVE BEHAVIOR

SLEEP DISTURBANCE

In this bipolar mania study, for those with psychotic symptoms, groups treated with ZYPREXA and divalproex showed comparable improvement in Y-MRS Total Score (ZYPREXA 42%, divalproex 43%;  $P=NS$ ).

ZYPREXA is indicated for the treatment of schizophrenia and acute bipolar mania.

For additional safety profile and other important prescribing considerations, see pages 16-17 and full Prescribing Information. Also, see pages 18-19 for Methodology and Study Limitations. For safety information on risperidone or divalproex, see manufacturers' package inserts.

<sup>1</sup> Tohen M, et al. *Am J Psychiatry* 2002;159(9):1011-1017.

<sup>2</sup> Data on file, Lilly Research Laboratories.

<sup>†</sup> Y-MRS is Young Mania Rating Scale, consisting of 11 items.

LOCF is Last Observation Carried Forward.

Mean modal doses were 17 mg/day for ZYPREXA and 1400 mg/day for divalproex.

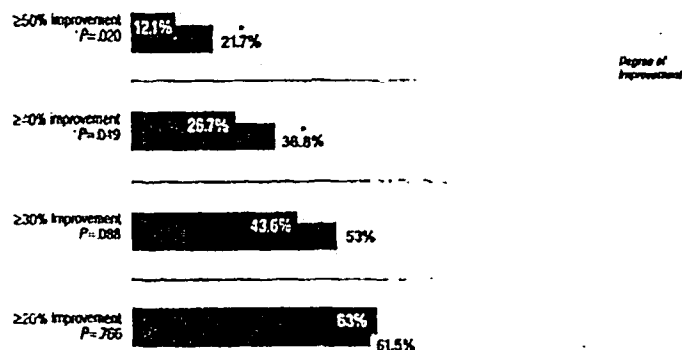
**ZYPREXA**  
Olanzapine

Bring comfort to residents' lives

# Significance to residents' lives.

Predictable

## Efficacy in total symptom improvement<sup>1</sup>



■ Risperidone (n=165)  
■ ZYPREXA (n=166)

% Patients Improving in PANSS Total Score  
from baseline to endpoint (LOCF)

## Symptoms

include:

HOSTILITY  
DELUSIONS  
EXCITEMENT  
HALLUCINATORY  
BEHAVIOR

In this schizophrenia study, a significantly greater percentage of patients treated with ZYPREXA achieved an improvement of ≥40% in PANSS Total Score as compared with risperidone-treated patients.

ZYPREXA is indicated for the treatment of schizophrenia and acute bipolar mania.

For additional safety profile and other important prescribing considerations, see pages 16-17 and full Prescribing Information. Also, see pages 18-19 for Methodology and Study Limitations. For safety information on risperidone, see manufacturer's package insert.

<sup>1</sup> Tren PL, et al. *J Clin Psychopharmacol*. 1997;17:407-418.

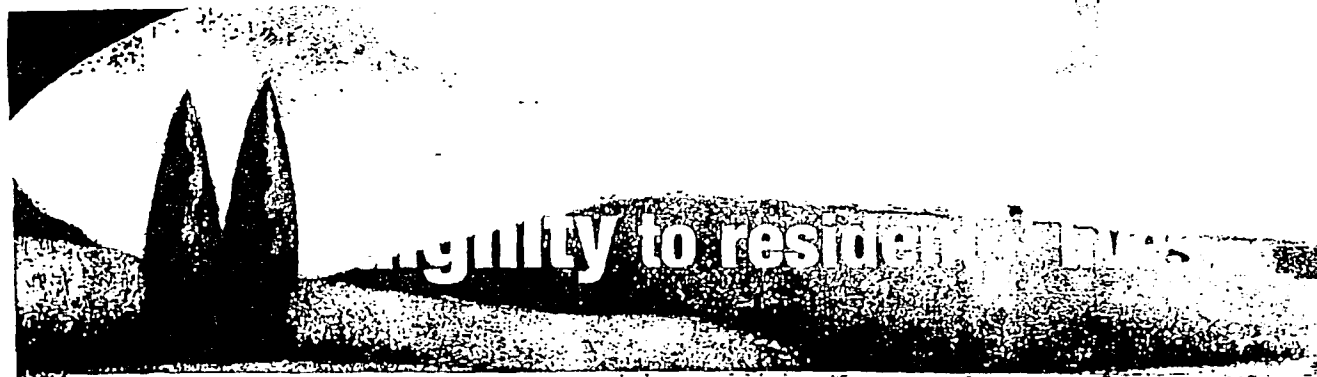
...dignity to residents' lives...

Bring comfort

Customize care

**zyprexa**  
Olanzapine





Predictable

Dependable maintenance

Dependable

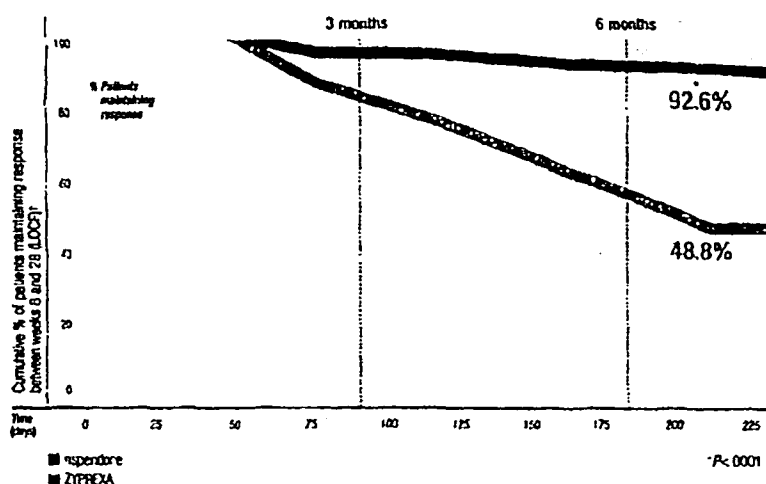
of treatment response in schizophrenia  
helps you **bring comfort.**





# 19% relapse urgency to residents' lives

## Superior maintenance of treatment response<sup>1,2</sup>



### Understanding OBRA†

#### 6 months

- ✓ Reevaluate patients
- ✓ No requirement for mandatory dose reduction

In this schizophrenia study, significantly fewer patients who reached more robust levels of improvement ( $\geq 40\%$ ) taking ZYPREXA experienced relapses at 28 weeks, compared to patients taking risperidone.

Significantly more patients taking ZYPREXA who had  $\geq 20\%$  improvement in PANSS Total Score at week 8 maintained their clinical response through week 28 (ZYPREXA 87.9%,  $n=105$ ; risperidone 67.7%,  $n=94$ ;  $P=.001$ ).<sup>1,2</sup>

Patients should be periodically reassessed to determine the need for maintenance treatment with appropriate dose.

ZYPREXA is indicated for the treatment of schizophrenia and acute bipolar mania.

For additional safety profile and other important prescribing considerations, see pages 16-17 and 18.9 Prescribing Information. Also, see pages 18-19 for Methodology and Study Limitations. For safety information on risperidone, see manufacturer's package insert.

1. Tran PY, et al. *J Clin Psychopharmacol* 1997;17:407-418.


2. Data on file, Lilly Research Laboratories.

† Response defined as  $\geq 40\%$  improvement in PANSS Total Score at week 8 (ZYPREXA  $n=44$ , risperidone  $n=37$ ). Relapse defined as  $\geq 20\%$  worsening in PANSS Total Score plus CGI-S  $\geq 3$  after 8 weeks.


‡ The Omnibus Budget Reconciliation Act (OBRA) guidelines for the use of antipsychotics were released in 1987.

Customize care

**ZYPREXA**  
olanzapine




Dignity to residents




Predictable

Flexible dosing



Dependable

helps you **customize care.**



Flexible

19 1/2 19 1/2 19 1/2

# Dignity to residents' lives

## ZYPREXA tablets

Once-daily dosing without regard to meals.

Starting dose of 5 mg recommended in patients  $\geq 65$  years of age.

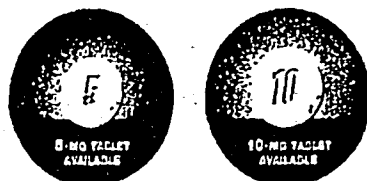


## ZYPREXA® Zydis® (olanzapine) Orally Disintegrating Tablets

Quickly dissolves orally in as little as 5 seconds.

When symptoms potentially lead to noncompliance (cheekers, spitters).

When residents are having difficulty swallowing medications.



**Phenylethanamines:** ZYPREXA Zydis contains phenylethylamine. Zydis is a registered trademark of R.P. Scherer Corporation.

Caution should be used in dosing to the elderly, especially if there are other factors that might additively influence drug metabolism and/or pharmacodynamic sensitivity.

ZYPREXA is indicated for the treatment of schizophrenia and acute bipolar mania.

For additional safety profile and other important prescribing considerations, see pages 16-17 and full Prescribing Information.

**ZYPREXA**  
olanzapine

# Threats to residents' lives.

Predictable

## Favorable safety profile

Dependable

### Low potential for harmful drug interactions if concomitant use is necessary

Little potential shown *in vitro* to inhibit P450 cytochromes:

valproate	warfarin	theophylline	diazepam
Lithium	biperiden	imipramine	

Coadministration of diazepam or ethanol with ZYPREXA may potentiate orthostatic hypotension. Lower doses of ZYPREXA should be considered in patients receiving concomitant treatment with fluvoxamine.

Flexible

### Low potential for cerebrovascular accidents

Only 0.12% of patients in placebo-controlled schizophrenia registration trials (patient ages 18-94) experienced treatment-emergent CVAs (3/2500).<sup>1</sup>

### Low potential for anticholinergic-like side effects

Incidence of common anticholinergic-like events not statistically different from placebo.<sup>1</sup>

Anticholinergic side effects may include: dry mouth, blurred vision, constipation, urinary retention, and increased heart rate.

### No baseline ECG required

No difference in clinically significant QTc prolongation with ZYPREXA compared to placebo in premarketing clinical trials.

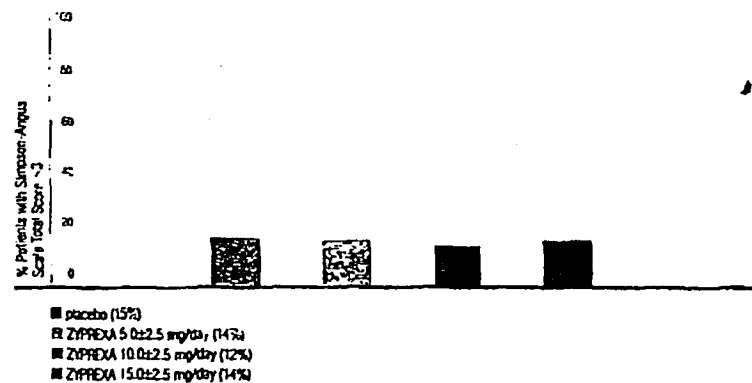
### No routine liver or kidney function tests required

### No adjustment of dosage required based upon degree of renal impairment

<sup>1</sup> Data on file, Lilly Research Laboratories.

<sup>2</sup> In patients with schizophrenia in 2 studies who had up to 6 weeks of therapy with ZYPREXA 2.5 to 17.5 mg/day (n=248) or with placebo (n=118).

# Incidence of EPS comparable to placebo



In placebo-controlled schizophrenia trials, the incidence of treatment-emergent extrapyramidal symptoms (EPS) associated with ZYPREXA was comparable to placebo,<sup>†</sup> as assessed by the Simpson-Angus Scale for Parkinsonism.<sup>‡</sup>

In only one analysis of a placebo-controlled study, only one specific form of EPS, akathisia, was reported significantly more often with ZYPREXA at any specific dose (10.0 $\pm$ 2.5 or 15.0 $\pm$ 2.5 mg/day) compared with placebo.

<sup>†</sup> Treatment-emergent EPS was analyzed in a double-blind, placebo-controlled comparison of ZYPREXA 5.0 $\pm$ 2.5, 10.0 $\pm$ 2.5, and 15.0 $\pm$ 2.5 mg/day with placebo and haloperidol 15.0 $\pm$ 5.0 mg/day involving 235 patients with schizophrenia. Results shown are for the 6-week acute phase.

<sup>‡</sup> No statistically significant differences vs placebo.

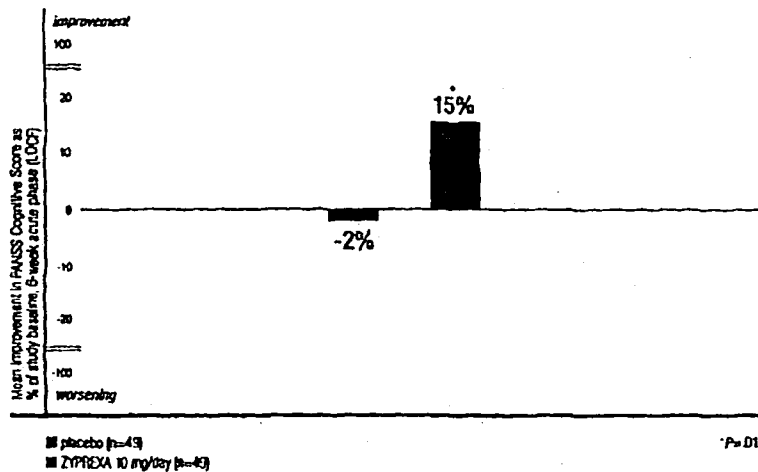
For additional safety profile and other important prescribing considerations, see pages 16-17 and for Prescribing Information. Also, see pages 18-19 for Methodology and Study Limitations.

**ZYPREXA**  
Olanzapine

significantly to residents' lives.

## ADDITIONAL DATA

No impairment in cognition<sup>†</sup>



Including:

ATTENTION  
ORGANIZED THINKING  
JUDGMENT AND  
INSIGHT

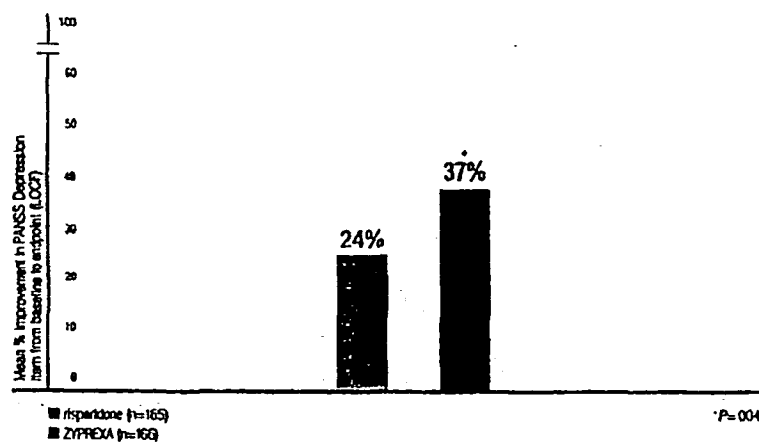
In this schizophrenia study, ZYPREXA significantly improved cognition as compared to placebo, as demonstrated by PANSS Cognitive Score.<sup>†</sup>

† Data on file, Lilly Research Laboratories.

† Results shown are from the 6-week acute phase of a double-blind comparison of ZYPREXA 1.0 and 10.0 mg/day with placebo, involving 152 patients with schizophrenia.

... dignity to residents' lives

### Efficacy in improving depressive symptoms<sup>1</sup>



#### Symptoms

Include:

SADNESS

HOPELESSNESS

In this schizophrenia study, ZYPREXA was significantly more effective than risperidone in improving depressive symptoms.

For additional safety profile and other important prescribing considerations, see pages 16-17 and full Prescribing Information. Also, see pages 18-19 for Methodology and Study Limitations. For safety information on risperidone, see manufacturer's package insert.

1. Tran PV, et al. J Clin Psychopharmacol. 1997;17:407-418.

**ZYPREXA**  
Olanzapine





## Prescribing ZYPREXA with dignity to residents' lives

### Transient, asymptomatic elevations of hepatic transaminase

In placebo-controlled schizophrenia studies, clinically significant ALT (SGPT) elevations ( $\geq 3$  times the upper limit of the normal range) were observed in 2% (6/243) of patients exposed to ZYPREXA compared to none (0/115) of the placebo patients. None of these patients experienced jaundice. Periodic assessment of transaminases is recommended in patients with significant hepatic disease.

As with all antipsychotic medications, the following considerations should be taken into account when prescribing ZYPREXA:

**Tardive dyskinesia (TD)**—prescribing should be consistent with the need to minimize the risk of TD. If its signs and symptoms appear, discontinuation should be considered.

**Seizures**—occurred infrequently in premarketing clinical trials of ZYPREXA (22/2500, 0.9%). Confounding factors may have contributed to many of these occurrences. ZYPREXA should be used cautiously in patients with a history of seizures or with conditions that lower the seizure threshold. Such conditions may be more prevalent in patients age 65 or older.

**Use in special populations**—In a clinical study involving nursing home patients having various psychiatric symptoms in association with Alzheimer's disease, somnolence, abnormal gait, fever, dehydration, and back pain were observed more often with ZYPREXA than with placebo. Of the 2500 patients in premarketing clinical studies with ZYPREXA, 11% (263) were 65 years of age or over. As with other CNS-active drugs, ZYPREXA should be used with caution in elderly patients with dementia. For patients of any age requiring special consideration, eg, patients who are debilitated, who are predisposed to hypotensive reactions, who have a combination of factors that may result in slower metabolism of ZYPREXA, or who may be more pharmacodynamically sensitive to ZYPREXA, a starting dose of 5 mg/day is recommended. When indicated, dose escalation should be performed with caution in these patients.

For additional safety profile and other important prescribing considerations, see the full Prescribing Information. For Methodology and Study Limitations, see pages 18-19.  
For safety information on risperidone or thioridazine, see manufacturers' package inserts.

**ZYPREXA**  
Olanzapine



**...ignity to residents' lives.**

## Methodology and study limitations

### ZYPREXA vs risperidone in schizophrenia

This was a double-blind, randomized, multicenter, international trial of 339 patients with schizophrenia, schizoaffective disorder, or schizophreniform disorder. Patients were randomized at a 1:1 ratio to treatment with ZYPREXA 10-20 mg/day or risperidone 4-12 mg/day. Patients enrolled in the study had the opportunity to complete 28 weeks of treatment. A total of 178 patients (52.5%) completed the study (ZYPREXA 57.6%; risperidone 47.3%;  $P=.059$ ).

- In this flexible-dose study, patients treated with ZYPREXA initiated therapy at 15 mg/day for the first 7 days of treatment. Thereafter, investigators could adjust the daily dose upward or downward by 5 mg/day every 7 days (range 10-20 mg) as clinically indicated. The mean modal dose for ZYPREXA was 17.2 mg/day.
- Consistent with labeling, risperidone-treated patients began titration at a dose of 1 mg twice daily on day 1, 2 mg twice daily on day 2, and 3 mg twice daily on days 3 through 7. Thereafter, investigators could adjust dose upward or downward by 2 mg/day every 7 days within the approved range of 4-12 mg/day as clinically indicated. The mean modal dose for risperidone was 7.2 mg/day.
- Treatment-emergent EPS was identified based on the following criteria: Simpson-Angus Scale total score  $>3$  at any post-baseline visit for subjects with baseline  $\leq 3$ ; Barnes Akathisia Scale global score  $\geq 2$  at any post-baseline visit for subjects with baseline  $<2$ .
- Patients who were previously exposed to risperidone were not excluded from this study, whereas patients previously exposed to ZYPREXA were.

### ZYPREXA vs divalproex in bipolar mania

This was a double-blind, randomized, acute-phase, 3-week study conducted in 44 US sites to compare the efficacy and safety of ZYPREXA vs divalproex. 251 patients with a DSM-IV diagnosis of bipolar I disorder experiencing acute mixed or manic episodes (baseline Young Mania Rating Scale [Y-MRS] Total Score  $\geq 20$ ), with or without psychotic features, with or without rapid cycling courses were included.

- Dosing ranges were 5-20 mg QD for ZYPREXA and 500-2500 mg divided for divalproex, with starting daily doses at 15 mg for ZYPREXA and 750 mg for divalproex. For the 3-week trial, mean modal doses were 17 mg for ZYPREXA and 1400 mg for divalproex; mean ending doses were 17 mg QD for ZYPREXA and 1500 mg divided for divalproex. Dosing adjustments could be made after 2 days and were based on clinical response and plasma levels. Plasma levels were performed to ensure divalproex trough levels were maintained within the targeted therapeutic range of 50-125  $\mu\text{g/mL}$ . Up to 4 blood samples were obtained per patient (mean, 2.7 samples); the mean value of all levels obtained was 79.4  $\mu\text{g/mL}$ .

# Restoring Dignity to residents' lives

PANSS Total Score Individual Items include: delusions, conceptual disorganization, hallucinatory behavior, excitement, grandiosity, suspiciousness/persecution, hostility, blunted affect, emotional withdrawal, poor rapport, passive/apathetic social withdrawal, difficulty in abstract thinking, lack of spontaneity and flow of conversation, stereotyped thinking, somatic concern, anxiety, guilt feelings, tension, mannerisms and posturing, depression, motor retardation, uncooperativeness, unusual thought content, disorientation, poor attention, lack of judgment and insight, disturbance of volition, poor impulse control, preoccupation, and active social avoidance. The items are rated on a 7-point scale from 1 (absent) to 7 (extreme).

Y-MRS Individual Items include: elevated mood, increased motor activity/energy, sexual interest, sleep, irritability, speech (rate and amount), language/thought disorder, thought content, disruptive/aggressive behavior, appearance, and insight.

Simpson-Angus Scale for Parkinsonism is used to measure drug-induced parkinsonism. Items include: gait, arm dropping, shoulder shaking, elbow rigidity, wrist rigidity, leg pendulousness, head dropping, glabellar tap, tremor, and salivation. Items are rated on a 5-point scale from 0 (complete absence of condition) to 4 (presence of condition in extreme form).

PANSS Cognitive Score includes: conceptual disorganization, difficulty in abstract thinking, stereotyped thinking, tension, mannerisms and posturing, poor attention, and lack of judgment and insight.

PANSS Depression Item measures depressive symptoms including sadness and hopelessness.

For additional safety profile and other important prescribing considerations, see pages 16-17 and full Prescribing Information. For safety information on risperidone or divalproex, see manufacturers' package inserts.

**ZYPREXA**  
Olanzapine

**Welcoming former  
military to residents' lives.**

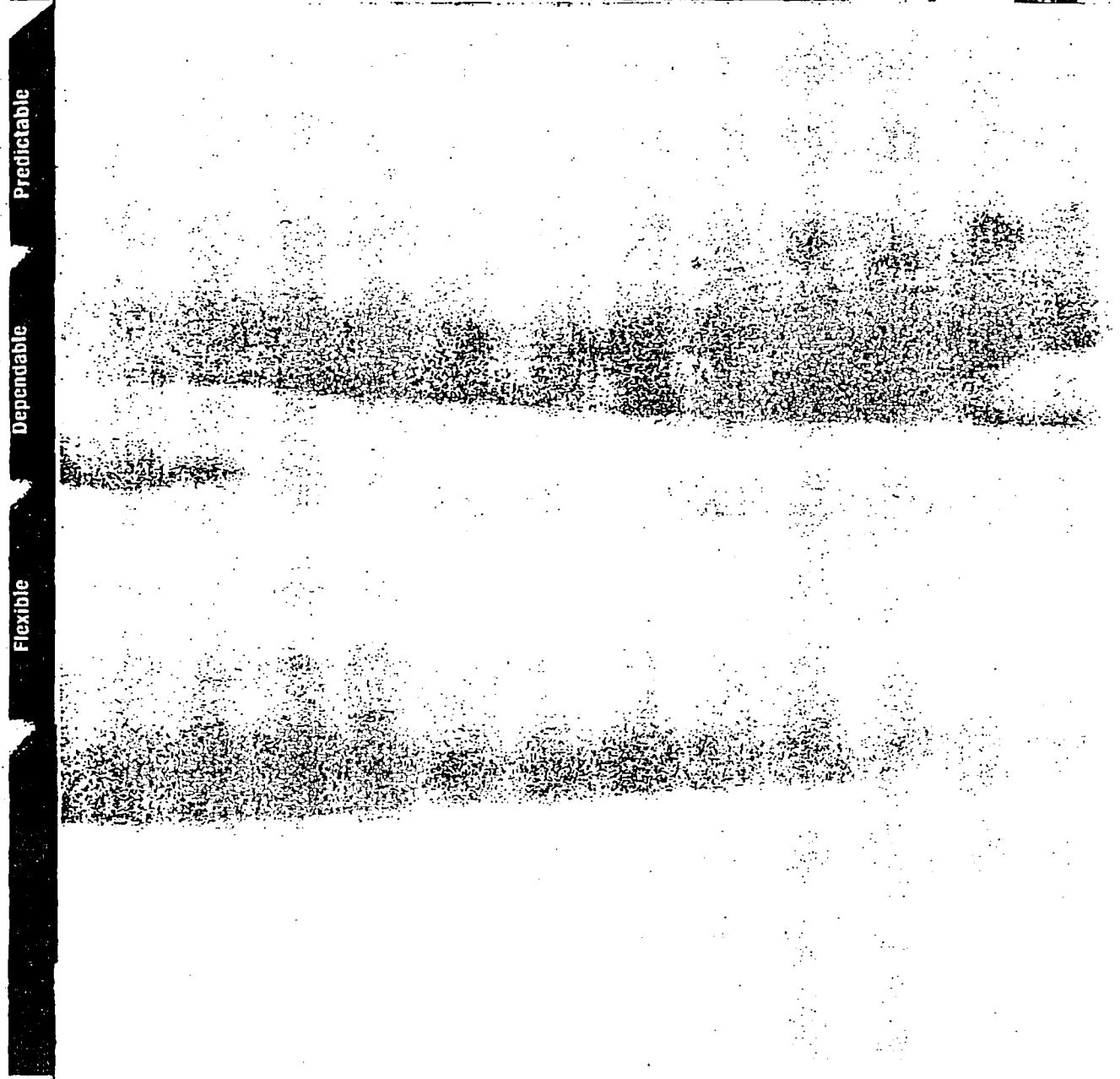
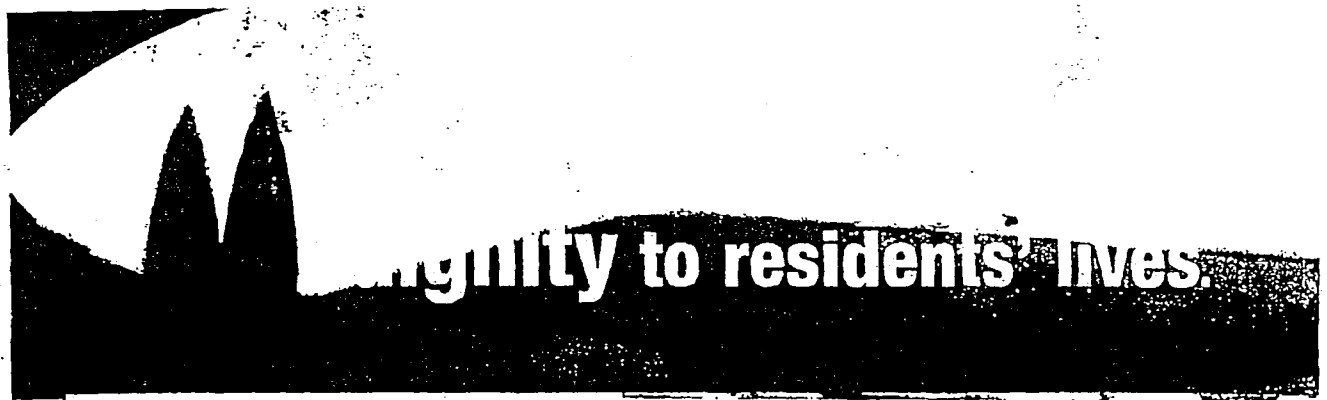
Predictable

Dependable

Flexible

... dignity to residents' lives

**zyprexa**  
Olanzapine

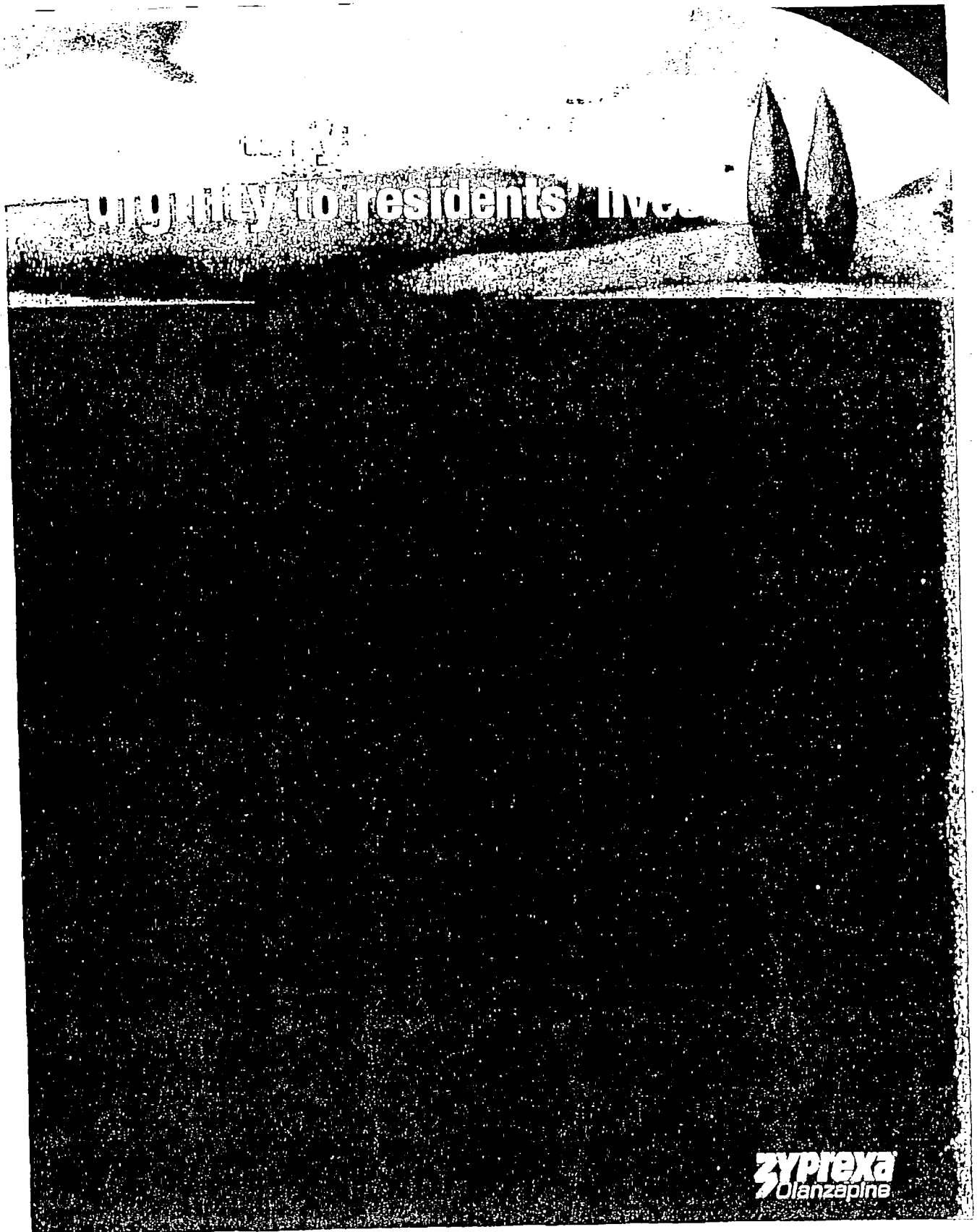


Predictable

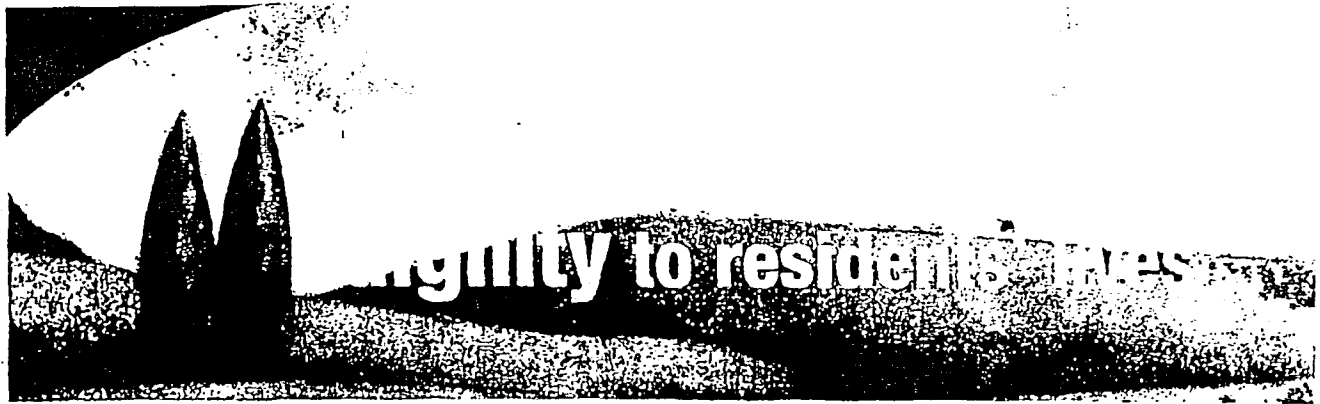
Dependable

Flexible





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Prescribed for more than 10 million patients worldwide.

[www.ZYPREXA.com](http://www.ZYPREXA.com)

Please see accompanying full Prescribing Information.

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HELPING MOVE LIVES FORWARD

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